in polarization energy in forming charge carriers. The majority carriers are electrons. Weak epr signals whose intensity follows Curie's law can be attributed entirely to impurity nickel thiete monoanions in the lattice.

Acknowledgments. This research was supported in part by the National Science Foundation Grants GP-8055 and GP-6656, for which we are grateful. R. D. S. wishes to thank the National Aeronautics and Space Agency for a Predoctoral Research Fellowship.

Complexation Kinetics of Sarcosine with Nickel(II), Cobalt(II), and Copper(II)[1]

R. F. Pasternack, K. Kustin,[2] L. A. Hughes, and E. Gibbs

Contribution from the Department of Chemistry, Ithaca College, Ithaca, New York 14850. *Received December 6, 1968*

Abstract: The kinetics of sarcosine complexation with nickel(II), cobalt(II), and copper(II) have been determined by temperature jump. The reactions were of the type $ML_{n-1} + L \rightleftharpoons ML_n(k_n, k_{-n})$, where $M = Ni^{2+}$, Co^{2+}, or Cu^{2+}, L refers to the anionic form of the ligand, and $n = 1, 2$, or 3. At ionic strength 0.1 *M* and 25° the rate constants are: Ni^{2+}, $k_1 = 1.3 \times 10^4\ M^{-1}\ sec^{-1}$, $k_{-1} = 4.1 \times 10^{-2}\ sec^{-1}$, $k_2 = 1.2 \times 10^4\ M^{-1}\ sec^{-1}$, $k_{-2} = 0.50\ sec^{-1}$, $k_3 \sim 5 \times 10^3\ M^{-1}\ sec^{-1}$, $k_{-3} \sim 5\ sec^{-1}$; Co^{2+}, $k_1 = 9.2 \times 10^5\ M^{-1}\ sec^{-1}$, $k_{-1} = 57\ sec^{-1}$, $k_2 = 1.5 \times 10^6\ M^{-1}\ sec^{-1}$, $k_{-2} = 5.7 \times 10^2\ sec^{-1}$; Cu^{2+}, $k_1 = 2.8 \times 10^9\ M^{-1}\ sec^{-1}$, $k_{-1} = 32\ sec^{-1}$, $k_2 = 1.0 \times 10^8\ M^{-1}\ sec^{-1}$, $k_{-2} = 22\ sec^{-1}$. The cobalt kinetics follow the dissociative mechanism for sarcosine. However, in the nickel complexation kinetics, formation of the mono and bis complexes appears to be relatively slow, indicating that the N-bonded methyl group in sarcosine has an influential role. As observed with cobalt, formation of the copper-sarcosinate complex is normal. Unlike cobalt, the formation of the bis complex is relatively slow.

The studies of nickel(II) and cobalt(II) with glycine,[3] the oligoglycines,[3] and glycylsarcosine[4] yielded several interesting results. First, for each of the metal ions, the same rate constant was obtained for the formation of the monosubstituted complexes ML, for L = glycylglycinate⁻, glycylglycylglycinate⁻, tetraglycinate⁻, or glycylsarcosinate⁻. (The values are $\sim 3 \times 10^5\ M^{-1}\ sec^{-1}$ for cobalt(II) and $\sim 2 \times 10^3\ M^{-1}\ sec^{-1}$ for nickel(II).) However, these values are appreciably smaller than the rate constants for the formation of the ML complex of glycine. The effect is more significant for nickel than for cobalt, the ratio of rate constants being 20 in the former case and 5 in the latter.

The rate constants for the formation of the bis species indicated further differences in the behavior of the two metal ions. For nickel(II), the observed rate constants were the same for all four peptides, and the ratio of the rate constants for the two complex formation steps (k_2/k_1) is greater than unity, actually about four. However, for cobalt(II), the observed rate constant, k_2, for glycylsarcosine is four times greater than that for the oligoglycines, with the rate constants for the oligoglycines in good agreement. Furthermore, the ratio of the rate constants, k_2/k_1, is slightly less than 1 for cobalt(II) with the oligoglycines. These results led us to conclude that the bonding model for cobalt-oligopeptide complexes is quite likely different from that for the nickel-oligopeptides.

To determine whether the presence of a methyl group at a binding site could account for the kinetic differences noted for the reactions of nickel(II) and cobalt(II) with glycylsarcosine, we have studied the complexation kinetics of these metal ions with sarcosine (N-methylglycine). We have also examined the copper(II)-sarcosine system, the results of which prove useful in interpreting the kinetics for the other two metal ions.

Experimental Section

The temperature-jump apparatus used for the present experiments was constructed by the Enfield Specialty Co. The temperature jump of nearly 10° was caused by discharging a 0.1-μF capacitor, charged to approximately 25 kV, through the solution. The rise time of the instrument was measured as 15 μsec at an ionic strength of 0.1 *M* using phenol red as indicator.

The light source is a Hanovia Division mercury-xenon arc lamp. The light passes through an interference filter, through the temperature-jump cell, and impinges upon a Dumont KM 2433 photomultiplier. The change in absorbancy which occurs as the equilibrium is shifted after the temperature jump is recorded on a storage oscilloscope and subsequently photographed.

The sarcosine used in these studies was obtained from Nutritional Biochemicals Corp. Baker reagent grade nitrate salts of potassium, cobalt, nickel, and copper were used. Stock solutions of the transition metal ions were prepared, and the concentrations of these solutions were determined using standard analytic techniques.

The indicators used in this study were Allied Chemical methyl orange, methyl red, chlorophenol red, and phenol red and Eastman Organic bromothymol blue.

Solutions were freshly prepared from solid sarcosine and stock solutions of KNO_3 and the appropriate metal ion and indicator. The solutions were degassed and the pH was adjusted by the dropwise addition of dilute NaOH and/or HNO_3 to ±0.01 pH unit.

Each relaxation time represents an average of at least three photographic determinations. The relative error for these measurements is ±10%. Test solutions of either metal ion or ligand in the absence of the other showed no discernible relaxation effects. These "blank" experiments were carried out at concentration levels of the free metal ion and ligand characteristic of solutions containing

---

[1] The authors gratefully acknowledge partial support from the Petroleum Research Fund for Grant 2982B and to the Public Health Service for Research Grant GM-08893-07 from the National Institute of General Medical Sciences, Public Health Service, to K. K.

[2] Department of Chemistry, Brandeis University, Waltham, Mass. 02154.

[3] G. Davies, K. Kustin, and R. F. Pasternack, submitted for publication.

[4] K. Kustin and R. F. Pasternack, *J. Phys. Chem.*, in press.

a mixture of the two. The rate constants obtained in this study are being reported to ±25% unless otherwise specified.

Results

Nickel. The reactions studied were of the type

$$\mathrm{ML}_{n-1} + \mathrm{L} \underset{k_{-n}}{\overset{k_n}{\rightleftharpoons}} \mathrm{ML}_n \qquad (1)$$

where n can equal 1, 2, or 3. The symbol "L" refers to the form of the ligand complexing with the metal ion, which, in these systems, is the anionic form (charges have been neglected for the sake of convenience). The analysis of the relaxation data requires a knowledge of the equilibrium constants for the system and the published equilibrium constants appropriate to these sarcosine systems are given in Table I. Only two stability constants had been reported for the nickel(II)–sarcosine system. However, it proved impossible to obtain a satisfactory fit to the kinetic data using a two-parameter system.[5] The possibility that the zwitterion is an attacking form of sarcosine was considered but discounted because this approach did not improve on the agreement between calculated and experimental relaxation times. That the zwitterion is not an attacking form of this α-amino acid with nickel(II) is consistent with the findings in previous studies.[6]

Table I. Equilibrium Constants (μ = 0.1 M, 25°)

$$K_1^{\mathrm{a}} = \frac{[\mathrm{H}^+][\mathrm{HL}]}{[\mathrm{H_2L}^+]} = 5.50 \times 10^{-3\,a}$$

$$K_2^{\mathrm{a}} = \frac{[\mathrm{H}^+][\mathrm{L}^-]}{[\mathrm{HL}]} = 9.77 \times 10^{-11\,a}$$

$$K_1^{\mathrm{Co}} = \frac{[\mathrm{CoL}^+]}{[\mathrm{Co}^{2+}][\mathrm{L}^-]} = 1.62 \times 10^{4\,b}$$

$$K_2^{\mathrm{Co}} = \frac{[\mathrm{CoL_2}]}{[\mathrm{CoL}^+][\mathrm{L}^-]} = 2.63 \times 10^{3\,b}$$

$$K_1^{\mathrm{Ni}} = \frac{[\mathrm{NiL}^+]}{[\mathrm{Ni}^{2+}][\mathrm{L}^-]} = 3.16 \times 10^{5\,a}$$

$$K_2^{\mathrm{Ni}} = \frac{[\mathrm{NiL_2}]}{[\mathrm{NiL}^+][\mathrm{L}^-]} = 2.40 \times 10^{4\,a}$$

$$K_1^{\mathrm{Cu}} = \frac{[\mathrm{CuL}^+]}{[\mathrm{Cu}^{2+}][\mathrm{L}^-]} = 8.71 \times 10^{7\,a}$$

$$K_2^{\mathrm{Cu}} = \frac{[\mathrm{CuL_2}]}{[\mathrm{CuL}^+][\mathrm{L}^-]} = 4.46 \times 10^{6\,a}$$

$$K_{\mathrm{In_i}} = \frac{[\mathrm{H}^+][\mathrm{In_i}^-]}{[\mathrm{HIn_i}]}$$

$\mathrm{HIn_i}$ =	$K_{\mathrm{In_i}}$ =
methyl orange	$3.47 \times 10^{-4\,c}$
methyl red	$1.00 \times 10^{-5\,c}$
chlorophenol red	$1.00 \times 10^{-6\,c}$
bromothymol blue	$7.94 \times 10^{-8\,c}$
phenol red	$1.55 \times 10^{-8\,c}$

[a] F. Basolo and Y. T. Chen, *J. Am. Chem. Soc.*, **76**, 953 (1954). [b] S. P. Datta, R. Leberman, and B. R. Rabin, *Trans. Faraday Soc.*, **55**, 1982 (1959). Stability constants corrected to ionic strength of 0.1 M. [c] I. M. Kolthoff, *J. Phys. Chem.*, **34**, 1466 (1930).

However, good agreement could be obtained between calculated and observed relaxation times when the formation of a tris complex was permitted (*cf.* Table II). Values of k_3 and k_{-3} were guessed and then fit to the kinetic data. The quotient of these values is, of course, K_3^{Ni}, which serves as the basis for a recalculation of the concentration in the system, from which another set of rate constants could again be obtained to fit the data. The "best-fit" rate constants for formation of the tris complex are shown in Table II. The value of the stability constant is in reasonable agreement with known constants of similar systems.[7] The rate constants are shown in Table II; the values of k_1 and k_2 are determined to ±25% but k_3 is less precisely known.

Table II. Relaxation Spectra of Nickel(II)–Sarcosine Solutions[a]

$[\mathrm{Ni}^{2+}]_0 \times 10^3$	$[\mathrm{Sarcosine}]_0 \times 10^3$	pH	τ_{obsd}, msec	τ_{calcd}, msec
2.50	2.84	8.45	52	50[b]
2.50	6.03	8.48	53	49
2.50	8.01	8.50	47	51
5.00	8.04	8.53	35	28
5.00	8.05	7.00	76	81
5.00	10.0	6.94	69	70
5.00	12.1	8.53	27	29
8.00	8.17	7.01	73	61
8.00	12.6	6.98	43	42
13.5	1.56	6.82	260	280

$k_1 = 1.3 \times 10^4$ M^{-1} sec^{-1} $\quad$ $k_2 = 1.2 \times 10^4$ M^{-1} sec^{-1} $\quad$ $k_3 \sim 5 \times 10^3$ M^{-1} sec^{-1}

$k_{-1} = 4.1 \times 10^{-2}$ sec^{-1} $\quad$ $k_{-2} = 0.50$ sec^{-1} $\quad$ $k_{-3} \sim 5$ sec^{-1}

[a] All concentrations are molar. The subscript zero refers to the total stoichiometric concentration; μ = 0.1 M (25°). [b] This result was obtained by solving a 3 × 3 matrix equation graphically.

Cobalt. Only two stability constants had been reported for the cobalt(II)–sarcosine system as well (*cf.* Table I). However, for this metal ion, we were able to work at sufficiently low pH that the formation of a tris complex was relatively unimportant. Furthermore, at these low pH values, a large number of the solutions contained metal ion in large excess over the anionic form of the ligand. It therefore proved possible for us to obtain an independent value for the rate constant for zwitterion attack. Under the appropriate conditions, the only complexation reactions which need be considered are

$$\begin{aligned} \mathrm{Co}^{2+} + \mathrm{L}^- &\underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{CoL}^+ \\ \mathrm{Co}^{2+} + \mathrm{HL} &\underset{k_{-1}'}{\overset{k_1'}{\rightleftharpoons}} \mathrm{CoL}^+ + \mathrm{H}^+ \end{aligned} \qquad (2)$$

By applying standard techniques for deriving relaxation-time expressions, we determined that

$$\frac{1}{\tau} = Ak_1 + Bk_1' \qquad (3)$$

where

$$A = \frac{[\mathrm{Co}^{2+}]}{1+\alpha} + [\mathrm{L}^-] + \frac{1}{K_1^{\mathrm{Co}}}$$

$$B = \frac{\alpha[\mathrm{Co}^{2+}]}{1+\alpha} + [\mathrm{HL}] + \frac{1}{K_1^{\mathrm{Co}}K_2^{\mathrm{a}}}\left([\mathrm{H}^+] + \alpha\beta\frac{[\mathrm{CoL}^+]}{1+\alpha}\right) \qquad (4)$$

$$\alpha = \frac{[\mathrm{H}^+]}{K_2^{\mathrm{a}} + \beta[\mathrm{L}^-]}$$

$$\beta = \frac{K_{\mathrm{In}} + [\mathrm{H}^+]}{K_{\mathrm{In}} + [\mathrm{H}^+] + [\mathrm{In}^-]}$$

---

(5) G. G. Hammes and J. I. Steinfeld, *J. Am. Chem. Soc.*, **84**, 4639 (1962).

(6) J. C. Cassatt and R. G. Wilkins, *ibid.*, **90**, 6045 (1968).

(7) L. G. Sillén and A. E. Martell, "Stability Constants of Metal-Ion Complexes," The Chemical Society, London, 1964.

A plot of $(\tau B)^{-1}$ *vs.* AB^{-1} was made and is shown in Figure 1. The slope of this line is k_1 and the intercept is k_1'. From the plot, we find that $k_1 = 9.2 \times 10^5$ M^{-1} sec^{-1} and $k_1' \cong 0$. The complete set of kinetic data for the cobalt(II)–sarcosine system with the determined rate constants are shown in Table III.

Table III. Relaxation Spectra of Cobalt(II)–Sarcosine Solutions[a]

$[Co^{2+}]_0 \times 10^3$	$[\text{Sarcosine}]_0 \times 10^3$	pH	τ_{obsd}, msec	τ_{calcd}, msec
2.68	7.99	7.17	1.1	0.87
2.68	2.48	6.89	3.4	3.5
5.35	4.87	7.15	0.77	0.74
5.35	8.01	6.96	0.96	0.66
2.14	4.99	6.80	2.8	2.9
2.14	7.95	7.11	1.6	1.0
2.14	1.98	7.08	3.5	3.9
1.61	1.98	6.86	4.9	5.9
1.61	1.45	6.79	8.4	7.4
1.07	2.07	7.23	4.4	3.4
8.03	9.32	5.80	3.6	4.1
10.7	12.4	6.25	0.80	1.0
13.4	9.93	6.05	0.77	1.4
13.4	0.988	6.07	6.2	7.7
1.07	5.01	8.04	1.5	0.75
2.67	50.8	7.11	0.43	0.45
2.67	71.9	7.05	0.42	0.45
2.67	88.7	7.09	0.39	0.46
5.35	107	7.14	0.25	0.28
5.35	158	7.08	0.23	0.31

$k_1 = 9.2 \times 10^5$ M^{-1} sec^{-1} $\quad k_2 = 1.5 \times 10^6$ M^{-1} sec^{-1}
$k_{-1} = 57$ sec^{-1} $\quad k_{-2} = 570$ sec^{-1}

[a] All concentrations are molar. The subscript zero refers to the total stoichiometric concentration; $\mu = 0.1$ M (25°).

Copper. Once again, as shown in Table I, only two equilibrium constants have been reported for copper(II). However, this is very likely an accurate description of the copper–sarcosine system. It was indeed found that two kinetic parameters were sufficient to fit the kinetic data.

It is only quite recently that copper complexation reactions have begun to be intensively studied using the temperature-jump technique.[8] This metal is so highly labile that the relaxation times for solutions whose pH is even within three units of the p*K* of the ligand fall outside the time range of this technique. It is often possible, however, to obtain relaxation data for solutions in which the pH is four to six units below the p*K* of the ligand, thus, in effect, slowing the reaction.

It would prove very valuable to treat the copper kinetic data in the same manner in which we analyzed the cobalt data. In this way an independent value of the rate constant for zwitterion attack could be obtained if it were appreciable. However, relaxation times were obtained only for those solutions in which both Cu^{2+} and CuL^+ were significant metal-containing species, precluding this treatment. Therefore, we can only report that the rate constant for zwitterion attack must be quite small, since it proved possible to fit the kinetic data without the introduction of kinetic terms involving the neutral ligand or any hypothetical species $CuOH^+$. The kinetic results and determined rate constants are given in Table IV.

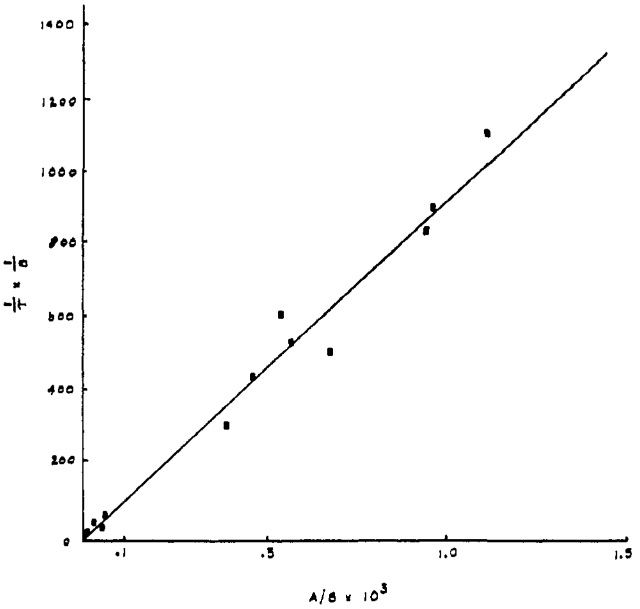

Figure 1. Plot of $(\tau B)^{-1}$ *vs.* AB^{-1} for cobalt(II)–sarcosine system. See text for definitions of *A* and *B*. The slope of this line is k_1 and the intercept is k_1', both in units of M^{-1} sec^{-1}.

Table IV. Relaxation Spectra of Copper(II)–Sarcosine Solutions[a]

$[Cu^{2+}]_0 \times 10^3$	$[\text{Sarcosine}]_0 \times 10^3$	pH	τ_{obsd}, msec	τ_{calcd}, msec
0.984	1.00	4.11	27	18
2.46	8.01	4.18	5.5	4.5
4.92	8.04	4.12	3.1	3.1
7.38	8.03	4.12	2.2	2.2
0.984	8.00	5.13	0.71	0.99
2.46	8.00	5.12	0.47	0.47
4.92	7.99	5.01	0.22	0.29
0.492	8.03	5.17	1.4	1.3
2.46	15.0	4.22	5.1	3.9
2.46	12.9	4.11	7.1	5.2

$k_1 = 2.8 \times 10^9$ M^{-1} sec^{-1} $\quad k_2 = 1.0 \times 10^8$ M^{-1} sec^{-1}
$k_{-1} = 32$ sec^{-1} $\quad k_{-2} = 22$ sec^{-1}

[a] All concentrations are molar. The subscript zero refers to the total stoichiometric concentration; $\mu = 0.1$ M (25°).

Discussion

The most recent determination of k_1 for the formation of the metal–glycine complex yields $k_1 = 1.5 \times 10^6$ M^{-1} sec^{-1} for cobalt(II) and $k_1 = 4.1 \times 10^4$ M^{-1} sec^{-1} for nickel(II).[3] These values, which are in better agreement with lifetime measurements of inner-coordination sphere water molecules,[9] were obtained by investigating the pH region significantly below the p*K* of the complexing ligand (see ref 8 for the application to otherwise often inaccessibly labile ions). It is therefore apparent that the value of k_1 determined for cobalt(II) with sarcosine (Table III) is somewhat smaller than the glycine value, but the difference is not significant, remaining within experimental error.

When the value of k_2 for cobalt(II) and sarcosine is compared with k_2 values for this metal ion with other α-amino acids, the agreement is also quite good. The values for sarcosine, glycine,[3] α-alanine,[10] and α-

---

(8) A. F. Pearlmutter and J. Stuehr, *J. Am. Chem. Soc.*, **90**, 858 (1968).

(9) T. J. Swift and R. E. Connick, *J. Chem. Phys.*, 41, 2553 (1964).

(10) K. Kustin, R. F. Pasternack, and E. M. Weinstock, *J. Am. Chem. Soc.*, **88**, 4610 (1966).

aminobutyric acid[11] are (in units of M^{-1} sec^{-1}) 1.5 × 10^6, 2.0 × 10^6, 0.8 × 10^6, and 1.9 × 10^6, respectively. We are led to conclude that cobalt(II)–sarcosine kinetics are entirely normal and that the presence of the N-methyl group has no significant effect on the complexation kinetics. This result is unexpected, as the methyl group is attached to a metal binding site. For example, comparison may be made with the effect of a methyl group on a nonbonding peptide nitrogen atom. It has been reported that the presence of the methyl group in glycylsarcosine leads to appreciable enhancement of water[3,4] loss from Co(glysar)$^+$ as compared to water loss from Co(glygly)$^+$.

If the N-methyl group exerts an inductive effect it would be expected that the dissociation rate constants for sarcosine would be less than those for glycine. The following are the experimental values for cobalt(II): k_{-1} = 34 sec^{-1} for glycine and 57 sec^{-1} for sarcosine; k_{-2} = 330 sec^{-1} for glycine, 570 sec^{-1} for sarcosine, 280 sec^{-1} for α-alanine, and 680 sec^{-1} for α-aminobutyric acid. As can be seen, the values are all in reasonable agreement, and if there is any trend at all it is in the direction of the dissociation constants being larger for sarcosine than for glycine.

The nickel results with sarcosine are more unusual than those of cobalt. Here, the k_1 value is a factor of 3 smaller than that obtained for glycine. As for k_2 values, they are for sarcosine, glycine,[3] α-alanine,[10] and α-aminobutyric acid[11] (in M^{-1} sec^{-1}) 1.2 × 10^4, 5.6 × 10^4, 4.0 × 10^4, and 1.5 × 10^4, respectively. Apparently, the presence of the methyl group on the terminal nitrogen interferes with the formation of the ML species and also the ML$_2$ species. Values of k_3 have been obtained for nickel(II) with glycine and sarcosine. For nickel, the value is 4 × 10^4 M^{-1} sec^{-1} with glycine and is estimated at 5 × 10^3 M^{-1} sec^{-1} for sarcosine.

A simple dissociative mechanism cannot account for these observations. On the other hand, water loss would be expected to remain rate determining, unless a ligand-based steric effect were present. In the latter case, labile ions are more influenced than less labile ions, a situation clearly inconsistent with the present study, as shown by the copper results. For the copper–glycine system $k_1 = 4 \times 10^9$ M^{-1} sec^{-1},[8] and for copper–sarcosine $k_1 = 3 \times 10^9$ M^{-1} sec^{-1}; the two values are very close, ruling out the presence of a steric effect.

Variations on the dissociative mechanism leading to some ligand influence on the rate of substitution have already been discussed.[12,13] It is, however, important to recognize that this type of observation is associated with more slowly reacting ions, of which, for a divalent ion, nickel is one.

The relative slowness in nickel substitution has been ascribed to crystal field effects.[14,15] Nickel(II) is exceptionally stable in the ground state, which increases the activation energy relative to the five-coordinate transition state. Moreover, the metal–ligand bonds in nickel are relatively short in amino acid compounds.[16] Consequently, two factors may influence the rate. (1) The substitution may be slow enough to afford time for ligand–water interactions in the inner sphere to play a role.[13] (2) Occupation of the coordination site may be retarded by the exacting requirements of the fit at the binding site.[17]

Finally, it is worth noting that $k_2 < k_1$ for copper, parallelling the glycine kinetics.[8] The observation may result from the inhibition of inversion when a bidentate ligand is present in the inner-coordination sphere. Further direct experimental evidence is necessary before it is possible to account for the source of this decrease in the relative ease of formation of higher order complexes characteristic of most other divalent transition metal ions with ligands of this type.

---

[11] A. Kowalak, K. Kustin, R. F. Pasternack, and S.Petrucci, *J. Am. Chem. Soc.*, **89**, 3126 (1967).

[12] C. H. Langford and H. B. Gray, "Ligand Substitution Processes," W. A. Benjamin, Inc., New York, N. Y., 1965.

[13] D. B. Rorabacher, *Inorg. Chem.*, **5**, 1891 (1966).

[14] M. Eigen, *Ber. Bunsenges, Physik. Chem.*, **67**, 753 (1963).

[15] F. Basolo and R. G. Pearson, "Mechanisms in Inorganic Reactions," 2nd ed, John Wiley & Sons, Inc., New York, N. Y., 1967, p 147.

[16] H. C. Freeman, *Advan. Protein Chem.*, **22**, 257 (1967).

[17] G. Davies, K. Kustin, and R. F. Pasternack, *Int. J. Chem. Kinetics*, **1**, 43 (1969).